REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 15-27 will be active in the application subsequent to entry of this Amendment.

Submitted with this response is a new declaration attending to the points of information mentioned in item 3 of the Official Action.

The claims have been amended in order to more particularly point out and distinctly claim that which applicants regard as their invention, to correct an error in the structure of formula (I) and to address claim clarity issues noted by the examiner in items 6-7 of the Official Action.

For convenience, the original set of claims has been deleted and a new set, claims 15-27, supplied. Claims 1-9 are replaced with new claims 15-23 and claim 10 has been deleted as being non-statutory. Original claims 11-14 have been revised and recast in traditional method of treatment style and now appear as new claims 24-27. These changes are responsive to the examiner's comments in items 8-9 of the Official Action.

In items 4 and 5 of the Official Action the examiner questions enablement for the original set of claims and in preparing this response applicant has noted a bond is missing from general formula (I) - this is apparent from claim 1, the structure on page 3 as well as the structure in the Abstract. All three of these structures have been amended to insert a double bond in the relevant formula.

It is emphasized that the applicant did not intend to include the non-hydrogenated camptothecins and this fact is evident from the specification and in particular from the preparation examples (examples 1-7) in which the compounds are prepared by the addition of protective groups and no reaction is undertaken in order to modify the camptothecin ring.

In fact, the applicant did not intend to seek protection for dihydrocamptothecins when the application was originally filed.

A person skilled in the art will appreciate that the preparation method unambiguously leads to the camptothecins belonging to the corrected general formula (I) since the process for their preparation is a one-step process wherein protective groups are added to the polyaminoalkyl residue in position-7.

The disclosed process does not include any reaction step that leads to the modification of the ring structure, and nowhere in the present application is there mentioned a step wherein such a bond could be reduced to obtain compounds corresponding to formula I as depicted in the document as filed.

As an example, the compounds described in example 1-page 8, example 2-page 9, example 4-page 10, example 5-page 11, example 6-page 11, and example 7-page12 all have as a starting material 7-formylcamptothecin which synthesis is described in the preparation process at page 7. This starting material is not a reduced analogue of camptothecin. The reactions relate to simple imine formation without any reducing agent.

Moreover, the synthesis of the compounds of example 3-page 9 start from already known compounds, which are not reduced analogues of camptothecin. The synthesis starts from 7-(3-aminopropoxyiminomethyl)-20S-camptothecin

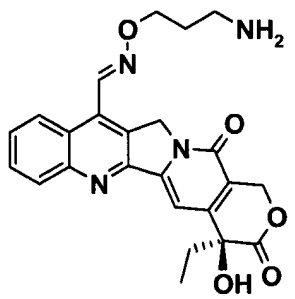


Figure 2

and consists of a simple Boc protection of this starting material.

The synthesis of the remaining claimed compounds can be found in J. Med. Chem. 1998, 41, 5410 as mentioned on page 5 of the present invention. The starting materials are not reduced analogues of camptothecin. As reported in page 5 "A second group of preferred compounds comprises formula (I) compounds with a 7-term lactone ring, the synthesis of which is described in J. Med. Chem. 1998, 41, 5410". The cited paper does not state or suggest anywhere a potential reduction of the C15-C16 double bond, but clearly describes the way the lactone ring is obtained (*see* page 5411, scheme 2).

In view of the above, the person skilled in the art will clearly understand that the double bond was erroneously overlooked in the application as filed and, by correcting it, the applicant

wishes to bring the claims, disclosure and abstract into conformity with the content of the description as originally filed, without adding new subject matter.

The Official Action also includes three separate rejections, items 11-13, based upon prior art. It would appear that these rejections are based upon the claims as originally submitted (which included an inadvertent error) but has now been corrected. The newly amended claim 15 does not include the compound disclosed in DallaValle 2001, Penco and Marzi since it include iminomethylcamptothecins having a protective group comprising a polyaminoalkil group where z and z' cannot be zero at the same time.

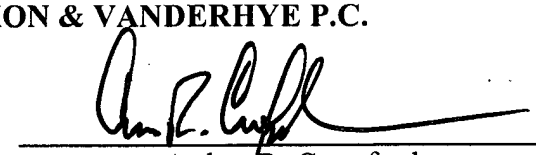
Withdrawal of these rejections is solicited.

The Official Action includes in items 15 and 16 two double patenting rejections based on U.S. 6,242,457 and 6,589,939, respectively. The amendments to the claims also resolves these two rejections and applicants request that they be withdrawn. Finally, the Official Action includes three provisional obviousness-type double patenting rejections over pending applications; *see* items 18-20. Applicants wish to have these provisional rejections held in abeyance until such time as allowable subject matter is indicated in this application or allowable subject matter is indicated in one of the three pending applications.

Should the examiner require further information, please contact the undersigned.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

Arthur R. Crawford
Reg. No. 25,327

ARC:eaw
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100